

## PART 225—CURRENT GOOD MANUFACTURING PRACTICE FOR MEDICATED FEEDS

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AUTHORITY: Secs. 501, 512, 701(a), 52 Stat. 1049-1050 as amended, 1055, 82 Stat. 343-351 (21 U.S.C. 351, 360(b), 371(a)).

SOURCE: 41 FR 52618, Nov. 30, 1976, unless otherwise noted.

### Subpart A—General Provisions

#### § 225.1 Current good manufacturing practice.

(a) Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act provides that a drug (including a drug contained in a medicated feed) shall be deemed to be adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirement of the act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess.

(b) The provisions of §§ 225.10 through 225.115, inclusive, set forth the criteria for determining whether the manufacture of a medicated feed is in compliance with current good manufacturing practice. These regulations shall apply to all types of facilities and equipment used in the production of medicated feeds, and they shall also govern those instances in which failure to adhere to the regulations has caused nonmedicated feeds that are manufactured, processed, packed, or held to be adulterated. In such cases, the medicated feed shall be deemed to be adulterated within the meaning of section 501(a)(2)(B) of the act, and the nonmedicated feed shall be deemed to be adulterated within the meaning of 402(a)(2)(D).

#### § 225.10 Personnel.

(a) Qualified personnel and adequate personnel training and supervision are essential for the proper formulation, manufacture, and control of medicated feeds. Training and experience leads to proper use of equipment, maintenance of accurate records, and

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detection and prevention of possible deviations from current good manufacturing practices.

(b)(1) All employees involved in the manufacture of medicated feeds shall have an understanding of the manufacturing or control operation(s) which they perform, including the location and proper use of equipment.

(2) The manufacturer shall provide an on-going program of evaluation and supervision of employees in the manufacture of medicated feeds.

[41 FR 52618, Nov. 30, 1976, as amended at 42 FR 12426, Mar. 4, 1977]

### Subpart B—Construction and Maintenance of Facilities and Equipment

#### § 225.20 Buildings.

(a) The location, design, construction, and physical size of the buildings and other production facilities are factors important to the manufacture of medicated feed. The features of facilities necessary for the proper manufacture of medicated feed include provision for ease of access to structures and equipment in need of routine maintenance; ease of cleaning of equipment and work areas; facilities to promote personnel hygiene; structural conditions for control and prevention of vermin and pest infestation; adequate space for the orderly receipt and storage of drugs and feed ingredients and the controlled flow of these materials through the processing and manufacturing operations; and the equipment for the accurate packaging and delivery of a medicated feed of specified labeling and composition.

(b) The construction and maintenance of buildings in which medicated feeds are manufactured, processed, packaged, labeled, or held shall conform to the following:

(1) The building grounds shall be adequately drained and routinely maintained so that they are reasonably free from litter, waste, refuse, uncut weeds or grass, standing water, and improperly stored equipment.

(2) The building(s) shall be maintained in a reasonably clean and orderly manner.

(3) The building(s) shall be of suitable construction to minimize access

by rodents, birds, insects, and other pests.

(4) The buildings shall provide adequate space and lighting for the proper performance of the following medicated feed manufacturing operations:

(i) The receipt, control, and storage of components.

(ii) Component processing.

(iii) Medicated feed manufacturing.

(iv) Packaging and labeling.

(v) Storage of containers, packaging materials, labeling and finished products.

(vi) Routine maintenance of equipment.

**§ 225.36 Equipment.**

(a) Equipment which is designed to perform its intended function and is properly installed and used is essential to the manufacture of medicated feeds. Such equipment permits production of feeds of uniform quality, facilitates cleaning, and minimizes spillage of drug components and finished product.

(b)(1) All equipment shall possess the capability to produce a medicated feed of intended potency, safety, and purity.

(2) All equipment shall be maintained in a reasonably clean and orderly manner.

(3) All equipment, including scales and liquid metering devices, shall be of suitable size, design, construction, precision, and accuracy for its intended purpose.

(4) All scales and metering devices shall be tested for accuracy upon installation and at least once a year thereafter, or more frequently as may be necessary to insure their accuracy.

(5) All equipment shall be so constructed and maintained as to prevent lubricants and coolants from becoming unsafe additives in feed components or medicated feed.

(6) All equipment shall be designed, constructed, installed and maintained so as to facilitate inspection and use of cleanout procedure(s).

**§ 225.35 Use of work areas, equipment, and storage areas for other manufacturing and storage purposes.**

(a) Many manufacturers of medicated feeds are also involved in the manufacture, storage, or handling of products which are not intended for animal feed use, such as fertilizers, herbicides, insecticides, fungicides, rodenticides, and other pesticides. Manufacturing, storage, or handling of nonfeed and feed products in the same facilities may cause adulteration of feed products with toxic or otherwise unapproved feed additives.

(b) Work areas and equipment used for the manufacture or storage of medicated feeds or components thereof shall not be used for, and shall be physically separated from, work areas and equipment used for the manufacture of fertilizers, herbicides, insecticides, fungicides, rodenticides, and other pesticides unless such articles are approved drugs or approved food additives intended for use in the manufacture of medicated feed.

**Subpart C—Product Quality Control**

**§ 225.42 Components.**

(a) A medicated feed, in addition to providing nutrients, is a vehicle for the administration of a drug, or drugs, to animals. To ensure proper safety and effectiveness, such medicated feeds must contain the labeled amounts of drugs. It is necessary that adequate procedures be established for the receipt, storage, and inventory control for all such drugs to aid in assuring their identity, strength, quality, and purity when incorporated into products.

(b) The receipt, storage, and inventory of drugs, including undiluted drug components, medicated premixes, and semiprocessed (i.e., intermediate premixes, inplant premixes and concentrates) intermediate mixes containing drugs, which are used in the manufacture and processing of medicated feeds shall conform to the following:

(1) Incoming shipments of drugs shall be visually examined for identity and damage. Drugs which have been subjected to conditions which may have adversely affected their identity,

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strength, quality, or purity shall not be accepted for use.

(2) Packaged drugs in the storage areas shall be stored in their original closed containers.

(3) Bulk drugs shall be identified and stored in a manner such that their identity, strength, quality, and purity will be maintained.

(4) Drugs in the mixing areas shall be properly identified, stored, handled, and controlled to maintain their integrity and identity. Sufficient space shall be provided for the location of each drug.

(5) A receipt record shall be prepared and maintained for each lot of drug received. The receipt record shall accurately indicate the identity and quantity of the drug, the name of the supplier, the supplier's lot number or an identifying number assigned by the feed manufacturer upon receipt which relates to the particular shipment, the date of receipt, the condition of the drug when received, and the return of any damaged drugs.

(6) A daily inventory record for each drug used shall be maintained and shall list by manufacturer's lot number or the feed manufacturer's shipment identification number at least the following information:

(i) The quantity of drug on hand at the beginning and end of the work day (the beginning amount being the same as the previous day's closing inventory if this amount has been established to be correct); the quantity shall be determined by weighing, counting, or measuring, as appropriate.

(ii) The amount of each drug used, sold, or otherwise disposed of.

(iii) The batches or production runs of medicated feed in which each drug was used.

(iv) When the drug is used in the preparation of a semiprocessed intermediate mix intended for use in the manufacture of medicated feed, any additional information which may be required for the purpose of paragraph (b)(7) of this section.

(v) Action taken to reconcile any discrepancies in the daily inventory record.

(7) Drug inventory shall be maintained of each lot or shipment of drug by means of a daily comparison of the

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actual amount of drug used with the theoretical drug usage in terms of the semiprocessed, intermediate and finished medicated feeds manufactured. Any significant discrepancy shall be investigated and corrective action taken. The medicated feed(s) remaining on the premises which are affected by this discrepancy shall be detained until the discrepancy is reconciled.

(8) All records required by this section shall be maintained on the premises for at least one year after complete use of a drug component of a specific lot number or feed manufacturer's shipment identification number.

### § 225.58 Laboratory controls.

(a) The periodic assay of medicated feeds for drug components provides a measure of performance of the manufacturing process in manufacturing a uniform product of intended potency.

(b) The following assay requirements shall apply to medicated feeds:

(1) For feeds requiring approved Medicated Feed Applications (Form FD 1800) for their manufacture and marketing. At least three representative samples of medicated feed containing each drug or drug combination used in the establishment shall be collected and assayed by approved official methods, at periodic intervals during the calendar year, unless otherwise specified in this chapter. At least one of these assays shall be performed on the first batch using the drug. If a medicated feed contains a combination of drugs, only one of the drugs need be subject to analysis each time, provided the one tested is different from the one(s) previously tested.

(2) For feeds not requiring approved Medicated Feed Applications (Form FD 1300) for their manufacture and marketing. At least one representative sample of medicated feed containing each drug or drug combination used in the establishment shall be collected and assayed by approved Association of Official Analytical Chemists (AOAC) methods, or other appropriate analytical methods, at intervals no longer than 12 months, unless otherwise specified in this chapter. If a medicated feed contains a combination of drugs, only one of the drugs need be

subject to analysis each 12 months, provided the one tested is different from the one(s) previously tested.

(c) The originals or copies of all results of assays, including those from State Feed Control Officials and any other governmental agency, shall be maintained on the premises for a period of not less than 1 year after distribution of the medicated feed.

(d) Where the results of assays indicate that the medicated feed is not in accord with label specifications or is not within permissible assay limits as specified in this chapter, investigation and corrective action shall be implemented and an original or copy of the record of such action maintained on the premises.

(e) Corrective action shall include provisions for discontinuing distribution where the medicated feed fails to meet the labeled drug potency. Distribution of subsequent production of the particular feed shall not begin until it has been determined that proper control procedures have been established.

§ 225.65 Equipment cleanout procedures.

(a) Adequate cleanout procedures for all equipment used in the manufacture and distribution of medicated feeds are essential to maintain proper drug potency and avoid unsafe contamination of feeds with drugs. Such procedures may consist of cleaning by physical means, e.g., vacuuming, sweeping, washing, etc. Alternatively, flushing or sequencing or other equally effective techniques may be used whereby the equipment is cleaned either through use of a feed containing the same drug(s) or through use of drug free feedstuffs.

(b) All equipment, including that used for storage, processing, mixing, conveying, and distribution that comes in contact with the active drug component, feeds in process, or finished medicated feed shall be subject to all reasonable and effective procedures to prevent unsafe contamination of manufactured feed. The steps used to prevent unsafe contamination of feeds shall include one or more of the following, or other equally effective procedures:

(1) Such procedures shall, where appropriate, consist of physical means (vacuuming, sweeping, or washing), flushing, and/or sequential production of feeds.

(2) If flushing is utilized, the flush material shall be properly identified, stored, and used in a manner to prevent unsafe contamination of other feeds.

(3) If sequential production of medicated feeds is utilized, it shall be on a predetermined basis designed to prevent unsafe contamination of feeds with residual drugs.

Subpart D—Packaging and Labeling

§ 225.80 Labeling

(a) Appropriate labeling identifies the medicated feed, and provides the user with directions for use which, if adhered to, will assure that the article is safe and effective for its intended purposes.

(b)(1) Labels and labeling, including placards, shall be received, handled, and stored in a manner that prevents labeling mixups and assures that correct labeling is employed for the medicated feed.

(2) Labels and labeling, including placards, upon receipt from the printer shall be proofread against the Master Record File to verify their suitability and accuracy. The proofread label shall be dated, initialed by a responsible individual, and kept for 1 year after all the labels from that batch have been used.

(3) In those instances where medicated feeds are distributed in bulk, complete labeling shall accompany the shipment and be supplied to the consignee at the time of delivery. Such labeling may consist of a placard or other labels attached to the invoice or delivery ticket, or manufacturer's invoice that identifies the medicated feed and includes adequate information for the safe and effective use of the medicated feed.

(4) Label stock shall be reviewed periodically and discontinued labels shall be discarded.

**Subpart E—Records and Reports**

**§ 225.102 Master record file and production records.**

(a) The Master Record File provides the complete procedure for manufacturing a specific product, setting forth the formulation, theoretical yield, manufacturing procedures, assay requirements, and labeling of batches or production runs. The production record(s) includes the complete history of a batch or production run. This record includes the amounts of drugs used, the amount of medicated feed manufactured, and provides a check for the daily inventory record of drug components.

(b) The Master Record File and production records shall comply with the following provisions:

(1) A Master Record File shall be prepared, checked, dated, and signed or initialed by a qualified person and shall be retained for not less than 1 year after production of the last batch or production run of medicated feed to which it pertains. The Master Record File or card shall include at least the following:

(i) The name of the medicated feed.  
(ii) The name and weight percentage or measure of each drug or drug combination and each nondrug ingredient to be used in manufacturing a stated weight of the medicated feed.

(iii) A copy or description of the label or labeling that will accompany the medicated feed.

(iv) Manufacturing instructions or reference thereto that have been determined to yield a properly mixed medicated feed of the specified formula for each medicated feed produced on a batch or continuous operation basis, including mixing steps, mixing times and, in the case of medicated feeds produced by continuous production run, any additional manufacturing directions including, when indicated, the settings of equipment.

(v) Appropriate control directions or reference thereto, including the manner and frequency of collecting the required number of samples for specified laboratory assay.

(2) The original production record or copy thereof shall be prepared by

qualified personnel for each batch or run of medicated feed produced and shall be retained on the premises for not less than 1 year. The production record shall include at least the following:

(i) Product identification, date of production, and a written endorsement in the form of a signature or initials by a responsible individual.

(ii) The quantity and name of drug components used.

(iii) The theoretical quantity of medicated feed to be produced.

(iv) The actual quantity of medicated feed produced. In those instances where the finished feed is stored in bulk and actual yield cannot be accurately determined, the firm shall estimate the quantity produced and provide the basis for such estimate in the Master Record File.

(3) In the case of a custom formula feed made to the specifications of a customer, the Master Record File and production records required by this section shall consist either of such records or of copies of the customer's purchase orders and the manufacturer's invoices bearing the information required by this section. When a custom order is received by telephone, the manufacturer shall prepare the required production records.

(4) Batch production records shall be checked by a responsible individual at the end of the working day in which the product was manufactured to determine whether all required production steps have been performed. If significant discrepancies are noted, an investigation shall be instituted immediately, and the production record shall describe the corrective action taken.

(5) Each batch or production run of medicated feed shall be identified with its own individual batch or production run number, code, date, or other suitable identification applied to the label, package, invoice or shipping document. This identification shall permit the tracing of the complete and accurate manufacturing history of the product by the manufacturer.

**§ 225.110 Distribution records.**

(a) Distribution records permit the manufacturer to relate complaints to

specific batches and/or production runs of medicated feed. This information may be helpful in instituting a recall.

(b) Distribution records for each shipment of a medicated feed shall comply with the following provisions:

(1) Each distribution record shall include the date of shipment, the name and address of purchaser, the quantity shipped and the name of the medicated feed. A lot or control number, or date of manufacture or other suitable identification shall appear on the distribution record or the label issued with each shipment.

(2) The originals or copies of the distribution records shall be retained on the premises for not less than one year after the date of shipment of the medicated feed.

#### § 226.115 Complaint files.

(a) Complaints and reports of experiences of product defects relative to the drug's efficacy or safety may provide an indicator as to whether or not medicated feeds have been manufactured in conformity with current good manufacturing practices. These complaints and experiences may reveal the existence of manufacturing problems not otherwise detected through the normal quality control procedures. Timely and appropriate follow-up action can serve to correct a problem and minimize future problems.

(b) The medicated feed manufacturer shall maintain on the premises a file which contains the following information:

(1) The original or copy of a record of each oral and written complaint received relating to the safety and effectiveness of the product produced. The record shall include the date of the complaint, the complainant's name and address, name and lot or control number or date of manufacture of the medicated feed involved, and the specific details of the complaint. This record shall also include all correspondence from the complainant and/or memo-anda of conversations with the complainant, and a description of all investigations made by the manufacturer and of the method of disposition of the complaint.

(2) For medicated feeds requiring an approved Medicated Feed Application (Form FD-1800), records and reports of clinical and other experience with the drug shall be maintained and reported, appropriately identified with the number(s) of the Form FD-1800 to which they relate, to the Bureau of Veterinary Medicine, 5600 Fishers Lane, Rockville, MD 20857, in duplicate, pursuant to § 510.301 of this chapter.

### PART 226—CURRENT GOOD MANUFACTURING PRACTICE FOR MEDICATED PREMIXES

#### Subpart A—General Provisions

##### Sec.

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#### Subpart B—Construction and Maintenance of Facilities and Equipment

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#### Subpart E—Records and Reports

226.102 Master-formula and batch-production records.

226.110 Distribution records.

226.115 Complaint files.

**AUTHORITY:** Secs. 501, 701, 52 Stat. 1049-1050 as amended; 1055-1056 as amended (21 U.S.C. 351, 371).

**SOURCE:** 40 FR 14031, Mar. 27, 1975, unless otherwise noted.

#### Subpart A—General Provisions

§ 226.1 Current good manufacturing practice.

The criteria in §§ 226.10 through 226.115, inclusive, shall apply in determining whether the methods used in, or the facilities and controls used for the manufacture, processing, packing, or holding of a medicated premix con-

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form to or are operated or administered in conformity with current good manufacturing practice to assure that a medicated premix meets the requirements of the act as to safety, and has the identity and strength, and meets the quality and purity characteristics which it purports or is represented to possess, as required by section 501(a)(2)(B) of the act. The regulations in this Part 226 permit the use of precision, automatic, mechanical, or electronic equipment in the production of a medicated premix when adequate inspection and checking procedures or other quality control procedures are used to assure proper performance.

### **§ 226.10 Personnel.**

The key personnel and any consultants involved in the manufacture and control of the medicated premix shall have a background of appropriate education or appropriate experience or combination thereof for assuming responsibility to assure that the medicated premix has the proper labeling and the safety, identity, strength, quality, and purity that it purports to possess.

## **Subpart B—Construction and Maintenance of Facilities and Equipment**

### **§ 226.20 Buildings.**

Buildings in which medicated premixes are manufactured, processed, packaged, labeled, or held shall be maintained in a clear and orderly manner and shall be of suitable size, construction and location in relation to surroundings to facilitate maintenance and operation for their intended purpose. The building shall:

(a) Provide adequate space for the orderly placement of equipment and materials used in any of the following operations for which they are employed to minimize risk of mixups between different medicated premixes, their components, packaging, or labeling:

(1) The receipt, sampling, control, and storage of components.

(2) Manufacturing and processing operations performed on the medicated premix.

(3) Packaging and labeling operations.

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(4) Storage of containers, packaging materials, labeling, and finished products.

(5) Control laboratory operations.

(b) Provide adequate lighting and ventilation, and when necessary for the intended production or control purposes, adequate screening, dust and temperature controls, to avoid contamination of medicated premixes, and to avoid other conditions unfavorable to the safety, identity, strength, quality, and purity of the raw materials and medicated premixes before, during, and after production.

(c) Provide for adequate washing, cleaning, toilet, and locker facilities.

Work areas and equipment used for the production of medicated premixes or for the storage of the components of medicated premixes shall not be used for the production, mixing or storage of finished or unfinished insecticides, fungicides, rodenticides, or other pesticides or their components unless such materials are recognized as approved drugs intended for use in animal feeds.

### **§ 226.30 Equipment.**

Equipment used for the manufacture, processing, packaging, bulk shipment, labeling, holding, or control of medicated premixes or their components shall be maintained in a clean and orderly manner and shall be of suitable design, size, construction, and location to facilitate maintenance and operation for its intended purpose. The equipment shall:

(a) Be so constructed that any surfaces that come into contact with medicated premixes are suitable, in that they are not reactive, additive, or absorptive to an extent that significantly affects the identity, strength, quality, or purity of the medicated premix or its components.

(b) Be so constructed that any substance required for the operation of the equipment, such as lubricants, coolants, etc., may be employed without hazard of becoming an unsafe additive to the medicated premix.

(c) Be constructed to facilitate adjustment, cleaning, and maintenance, and to assure uniformity of production and reliability of control procedures and to assure the exclusion from medi-

cated premixes of contamination, including cross-contamination from manufacturing operations.

(d) Be suitably grounded electrically to prevent lack of uniform mixing due to electrically charged particles.

(e) Be of suitable size and accuracy for use in any intended measuring, mixing, or weighing operations.

#### Subpart C—Product Quality Control

##### § 226.40 Production and control procedures.

Production and control procedures shall include all reasonable precautions, including the following, to assure that the medicated premixes produced have the identity, strength, quality, and purity they purport to possess:

(a) Each critical step in the process, such as the selection, weighing, and measuring of components; the addition of drug components during the process; weighing and measuring during various stages of the processing; and the determination of the finished yield, shall be performed by one or more competent, responsible individuals. If such steps in the processing are controlled by precision, automatic, mechanical, or electronic equipment, their proper performance shall be adequately checked by one or more competent, responsible individuals.

(b) All containers to be used for undiluted drugs, drug components, intermediate mixtures thereof, and medicated premixes shall be received, adequately identified, and properly stored and handled in a manner adequate to avoid mixups and contamination.

(c) Equipment, including dust-control and other equipment, such as that used for holding and returning recovered or flush-out materials back into production, shall be maintained and operated in a manner to avoid contamination of the medicated premixes and to insure the integrity of the finished product.

(d) Competent and responsible personnel shall check actual against theoretical yield of a batch of medicated premix, and, in the event of any significant discrepancies, key personnel shall prevent distribution of the batch in question and other associated

batches of medicated premixes that may have been involved in a mixup with it.

(e) Adequate procedures for cleaning of those parts of storage, mixing conveying and other equipment coming in contact with the drug component of the medicated premix shall be used to avoid contamination of medicated premixes.

(f) If there is sequential production of batches of a medicated premix containing the same drug component (or components) at the same or lower levels, there shall be sufficient safeguards to avoid any buildup above the specified levels of the drug components in any of the batches of the medicated premix.

(g) Production and control procedures shall include provision for discontinuing distribution of any medicated premix found by the assay procedures, or other controls performed to fail to conform to appropriate specifications. Distribution of subsequent production of such medicated premix shall not begin until it has been determined that proper control procedures have been established.

##### § 226.42 Components.

(a) Drug components, including undiluted drugs and any intermediate mixes containing drugs used in the manufacture and processing of medicated premixes, shall be received, examined or tested, stored, handled, and otherwise controlled in a manner to maintain the integrity and identification of such articles. Appropriate receipt and inventory records shall be maintained for 2 years, and such records shall show the origin of any drug components, the manufacturer's control number (if any), the dates and batches in which they were used, and the results of any testing of them.

(b) Nondrug components shall be stored and otherwise handled in a manner to avoid contamination, including cross-contamination from manufacturing operations.

##### § 226.58 Laboratory controls.

Laboratory controls shall include the establishment of adequate specifications and test procedures to assure that the drug components and the



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medicated premixes conform to appropriate standards of identity, strength, quality, and purity. Laboratory controls shall include:

(a) The establishment of master records containing appropriate specifications and a description of the test procedures used to check them for each kind of drug component used in the manufacture of medicated premixes. This may consist of the manufacturer's or supplier's statement of specifications and methods of analyses.

(b) The establishment of specifications for medicated premixes and a description of necessary laboratory test procedures to check such specifications.

(c) Assays which shall be made of representative samples of finished medicated premixes in accordance with the following schedule:

(1) Each batch of a medicated premix manufactured from an undiluted drug shall be assayed for its drug component(s).

(2) In the case of medicated premixes which are manufactured by dilution of medicated premix(es) assayed in accordance with paragraph (c)(1) of this section, each batch shall be assayed for its drug component(s) with the first five consecutive batches assaying within the limitations, followed thereafter by assay of representative samples of not less than 5 percent of all batches produced. When any batch does not assay within limitations, each batch should again be assayed until five consecutive batches are within limitations.

(d) A determination establishing that the drug components remain uniformly dispersed and stable in the medicated premix under ordinary conditions of shipment, storage, and use. This may consist of a determination on a medicated premix of substantially the same formula and characteristics. Suitable expiration dates shall appear on the labels of the medicated premixes when needed to assure that the articles meet the appropriate standards of identity, strength, quality, and purity at the time of use.

(e) Adequate provision to check the reliability, accuracy, and precision of any laboratory test procedure used. The official methods in "Methods of

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Analysis of the Association of Official Analytical Chemists,"<sup>1</sup> methods described in an official compendium, and any method submitted as a part of a food additive petition or new-drug application that has been accepted by the Food and Drug Administration shall be regarded as meeting this provision.

(f) Provisions for the maintenance of the results of any assays, including dates and endorsement of analysts. Such records shall be retained in the possession of the manufacturer and shall be maintained for a period of at least 2 years after distribution by the manufacturer of the medicated premix has been completed.

**Subpart D—Packaging and Labeling**

**§ 226.80 Packaging and labeling.**

(a) Packaging and labeling operations shall be adequately controlled:

(1) To assure that only those medicated premixes that have met the specifications established in the master-formula records shall be distributed.

(2) To prevent mixups during the packaging and labeling operations.

(3) To assure that correct labeling is employed for each medicated premix.

(4) To identify medicated premixes with lot or control numbers that permit determination of the history of the manufacture and control of the batch of medicated premix.

(b) Packaging and labeling operations shall provide:

(1) For storage of labeling in a manner to avoid mixups.

(2) For careful checking of labeling for identity and conformity to the labeling specified in the batch-production records.

(3) For adequate control of the quantities of labeling issued for use with the medicated premix.

(c) Medicated premixes shall be distributed in suitable containers to insure the safety, identity, strength, and quality of the finished product.

<sup>1</sup> Copies may be obtained from: Association of Official Analytical Chemists, P.O. Box 540; Ben Franklin Station, Washington, DC 20044.

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**Subpart E—Records and Reports**

**§ 226.102 Master-formula and batch-production records.**

(a) For each medicated premix master-formula records shall be prepared, endorsed, and dated by a competent and responsible individual and shall be independently checked, reconciled, endorsed, and dated by a second competent and responsible individual. The record shall include:

(1) The name of the medicated premix and a specimen copy of its label.

(2) The weight or measure of each ingredient, adequately identified, to be used in manufacturing a stated weight of the medicated premix.

(3) A complete formula for each batch size, or of appropriate size in the case of continuous systems to be produced from the master-formula record, including a complete list of ingredients designated by names or codes sufficiently specific to indicate any special quality characteristics; an accurate statement of the weight or measure of each ingredient, except that reasonable variations may be permitted in the amount of ingredients necessary in the preparation of the medicated premix, provided that the variations are stated in the master formula; an appropriate statement concerning any calculated excess of an ingredient; and a statement of the theoretical yield.

(4) Manufacturing instructions for each type of medicated premix produced on a batch or continuous operation basis, including mixing steps and mixing times that have been determined to yield an adequately mixed medicated premix; and in the case of medicated premixes produced by continuous production run, any additional manufacturing directions including, when indicated, the settings of equipment that have been determined to yield an adequately mixed medicated premix of the specified formula.

(5) Control instructions, procedures, specifications, special notations, and precautions to be followed.

(b) A separate batch-production and control record shall be prepared for each batch or run of medicated premix

produced and shall be retained for at least 2 years after distribution by the manufacturer has been completed. The batch-production and control record shall include:

(1) Product identification, date of production, and endorsement by a competent and responsible individual.

(2) Records of each step in the manufacturing, packaging, labeling, and controlling of the batch, including dates, specific identification of drug components used, weights or measures of all components, laboratory-control results, mixing times, and the endorsements of the individual actively performing or the individual actively supervising or checking each step in the operation.

(3) A batch number that permits determination of all laboratory-control procedures and results on the batch and all lot or control numbers appearing on the labels of the medicated premix.

**§ 226.110 Distribution records.**

Complete records shall be maintained for each shipment of medicated premixes in a manner that will facilitate the recall, diversion, or destruction of the medicated premix, if necessary. Such records shall be retained for at least 2 years after the date of the shipment by the manufacturer and shall include the name and address of the consignee, the date and quantity shipped, and the manufacturing dates, control numbers, or marks identifying the medicated premix shipped.

**§ 226.115 Complaint files.**

Records shall be maintained for a period of 2 years of all written or verbal complaints concerning the safety or efficacy of each medicated premix. Complaints shall be evaluated by competent and responsible personnel and, where indicated, appropriate action shall be taken. The record shall indicate the evaluation and the action.